

SHATTUCK (F.C.)

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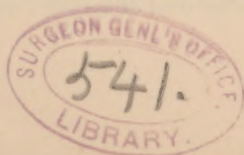
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FOUR CASES OF MYXÆDEMA TREATED BY THYROID EXTRACT.

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THE evolution of our knowledge of the functions of the thyroid gland and the interdependence of atrophy of the gland and the disease which, following Ord, we call myxœdema, will constitute, I think, one of the most interesting chapters of the medical history of our time. Cretinism, endemic and sporadic, had long been known when the late Sir William Gull, just twenty years ago, published his paper on "A Cretinoid State Supervening in Adult Life in Women." The next important step was taken when the Swiss surgeons, Kocher and Reverdin, recognized the identity in symptoms of the cases described by Gull and certain cases in which total extirpation of the thyroid gland for goitre had been practised. Then came the confirmatory experimental evidence derived from extirpation in animals, notably dogs and monkeys, and complete demonstration that the thyroid gland plays an extremely important rôle in the economy, profoundly influencing the nutrition of the central nervous system, and through it of the skin and its appendages in particular. Antiseptic surgery rendered the next step possible — the transplantation of the thyroid gland. Temporary improvement followed this procedure: but it was only temporary, as a rule, inasmuch as the gland underwent absorption instead of rooting itself and persisting as such. The disease thus remained of great clinical and pathological interest, but was considered practically not amenable to treatment. For instance, Osler's "Practice of Med-

¹ Read before the Boston Society for Medical Improvement, December 11, 1893.



icine," the prefatory note of which bears the date January 1, 1892, says: "Unfortunately, no satisfactory treatment is known. The patients suffer in cold and improve gradually in warm weather; they should therefore be kept at an even temperature and should, if possible, move to a warm climate in the winter months." How differently would this passage have been worded January 1, 1893!

To Dr. George Murray, of Newcastle, England, belongs the credit of the practical introduction of our present brilliantly successful treatment. In 1891, he began the hypodermic injection of a glycerine extract of the sheep's thyroid. The obvious dangers and inconveniences of this method led to the attempt to attain the same good results by the feeding of the raw gland, finely minced, to myxœdematous patients. *Mirabile dictu*, gastric and intestinal digestion were found not to impair the efficacy of the gland, and it was proved to be still active even when moderately cooked. Under these circumstances it is not to be wondered at that dried or liquid extracts of the gland, which offer convenient modes of administration, are found to be thoroughly effective. We are still much in the dark as to exactly what the gland does in the economy and how it does it, and we must probably look to physiological chemistry for the answer to these questions. The interest of the subject is so great that I have not been able to refrain from these introductory remarks to a brief report of four cases in private practice which I have thus far treated by thyroid extracts.

CASE I. This is, as far as I know, the first thus treated in this country, and presents some points of special interest. Miss A, twenty-nine years old, first consulted me April 21, 1892. Her maternal great-grandmother and great-aunt and her paternal grandmother died of cancer; otherwise the family history is

unimportant. The catamenia appeared during the thirteenth year, and were regular. She was well until she reached the age of seventeen, when she left school on account of frontal headache and nervousness. For the next five or six years she was anæmic and lacked strength. The catamenia diminished in amount and she had leucorrhœa; but she did much as other girls, nevertheless, and was fond of dancing, in which she excelled. In 1885, much arsenic was found in the cretonne and wall-paper of her room. These articles were removed, and she improved somewhat; but remained physically below par. In October, 1890, she took carbonate-of-iron pills, and by January 1, 1891, considered herself perfectly well. In January, 1891, normal menstruation appeared; February was skipped; in March, May and June there was a slight flow; but the period has been entirely absent ever since, nor has there been any return of the leucorrhœa. In February, 1891, she began to gain weight, and since then had put on twenty pounds, especially about the face and bust. The complexion, which was formerly fair and delicate, had become coarse and red, and her appearance had so changed that she was often not recognized. Within a few months the palms of the hands in particular, but also the soles of the feet and portions of the integument covering the neck and trunk, had acquired a peculiar yellow color. This could also be detected on the mucous membrane of the inner surface of the lips. The skin was generally rather coarse and rough, but was deeply fissured and cracked toward the finger-tips. The coloration of the fingers, combined with the roughness, led Dr. Osler, who saw her with me, to compare the skin to the covering of a goose's foot. The nails were brittle and uneven, the hair thin and dry. The patient herself questioned whether the color of the fingers could be

attributed to oranges, of which she had eaten many of late; but she observed that she could not wash or scrub the color off, and that it did not disappear when she temporarily omitted this fruit. She stated that three years ago, and several times since, she had awaked in the morning to find blisters (herpes?) on her nose. Lately she had had two small red bunches on her eyelids. One was removed by Dr. Cheney; the other disappeared spontaneously. Later she had another which I saw, and which looked like a sty, though it did not suppurate. Within two years a vaginal examination had been made by a competent hand, which discovered nothing amiss. In past years she had consulted specialists for her hair, and a throat specialist, and had been under the care of several physicians one after another.

Visceral examination was negative and the temperature normal. There was no mental or physical sluggishness; indeed, subsequent evidence would suggest that she was at this time mentally elated rather than depressed or indifferent. She was not strong; but complained chiefly of her changed appearance, coarse complexion and unevenly distributed gain in flesh. Perspiration was slight or absent. Her appetite was very large, digestion good, but sleep very poor, not more than four hours a night. I examined the blood, though I made no regular count, nor did I estimate the hæmoglobin. I considered it practically normal as did Dr. Osler some weeks later. The urine was normal in amount and not very significant. It contained constantly a very faint trace of albumen, uric-acid crystals, once a few hyaline casts, and a trace of arsenic ("A small trace in comparison with most cases of arsenical poisoning," Dr. Wood reported to me). Supraclavicular pads were present.

Suspecting myxœdema, though the case differed

decidedly from those I had seen or read of previously, I sent her to Dr. J. J. Putnam, providing that he should not know my opinion before he stated his own. He was inclined to call it obesity with menstrual disturbance, rather than myxœdema. A few weeks later Dr. Osler saw her, and concurred in my diagnosis. I then began injections of a glycerine extract of sheep's thyroid prepared for me with every precaution by Dr. A. C. Jelly, who visited the abattoir weekly himself, and kindly took infinite pains, thanks to which no undesirable local symptom was ever produced. The extract obtained from one gland was injected every week in three doses for about three months by myself and Dr. Charles Folsom, who kindly assumed charge of her during my vacation.

For the last year she has not been under my care, as she lives out of town and has been unable to come in. During this year she has taken the dried extract of Parke, Davis & Co., and is now taking the New York glycerine extract by the mouth. At first, there was improvement in the condition of the skin, but I now believe that was attributable to the warm weather rather than to the treatment, which has been of no real benefit to her. About the middle of May an ecchymosis appeared on the right thigh as large as a small lemon. She had received no blow or injury so far as she knew, and the injections were all made in the back. In August, 1892, she began to be depressed mentally, and several times tried to end her life; indeed, for the last year she has been watched incessantly. The chief effects attributable to the thyroid administration seem to be loss of flesh, strength and appetite. A number of months ago a swelling near the left angle of the jaw appeared and discharged pus.

Dr. Cutler, of Waltham, under whose care she now

is, kindly writes me that the left cheek is riddled with sinuses, and new abscesses occasionally form. He also says: "There is no violence, and apparently no hallucination or delusion, unless it may be a delusion when she says she cannot possibly move while almost in the act of walking. She is much depressed, and indeed quite desperate often, for she is certain she shall never be better. She has an intense præcordial distress often, which I judge to be the præcordial pain of melancholia. The hair is still falling, but new is growing. The skin and nails are still dry and rough. Speech is slow, but perfectly rational. She probably still retains her suicidal inclination, but does not manifest it in any way except in an occasional doubtful word."

Her mother writes under date of December 8, 1893: "There are black and blue marks on her legs, which, indeed, are so thin that they look like two sticks. Her face is swollen, also her waist, but the chest is hollow. The eyelids are swollen; the eyeballs often protrude. Her weight, which was 135 pounds when she first consulted you, is now less than 99. The under eye-lashes have gone. In July, 1892, her bust measured 40 inches; in October, 1893, 36 inches. In July, 1892, her waist measured 33 inches; in October, 1893, 29 inches."

I permit myself a few remarks on this case here, as it is sharply contrasted with the others which I am about to report. I confess that the failure of the appropriate treatment is a point against the correctness of the diagnosis of myxœdema in this case. If it be not myxœdema, I am at a loss what to call it. Dr. Mitchell Clark² reports two cases of failure, the only two I have been able to find in which treatment has been ineffectual. The treatment lasted two months

² British Medical Journal, August 27, 1892, p. 451.

and six weeks respectively. The use of these different thyroid preparations in my case, one after another, shows that the failure is not attributable to inertness of the remedy.

CASE II. Mr. B., sixty-nine years of age, consulted me first March 26, 1893. He has had many attacks of rheumatic iritis, and been quite deaf for a number of years. He at first dated his symptoms from about December, declaring that he had been perfectly well the previous summer. Later he, and especially his wife, felt sure that the symptoms were of older date, and had been gradually coming on for at least a year, though more rapidly of late. He said he was suffering from "a dropsical tendency," and wished relief for two symptoms, — a nearly constant watering of the eyes and serous running from the nose, and an unsatisfactory condition of the bowels which moved once daily, the dejections being small and watery. I found that he was notably weak, so much so that he had not for some weeks made his accustomed daily visit to his club, only a few steps from the house. He had become very sensitive to cold, and would sit before the fire with his feet in a foot-muff and in a temperature of the room which was trying to his family. A sensation as if the lining membrane of his mouth and throat were swollen was also mentioned. Perspiration was absent. The skin of the hands was very dry and rough, the nails brittle; and he said his hands felt stiff when trying to grasp anything. The integument generally was dry and harsh, though far less so than the hands, and his skin had previously been unusually soft and smooth. There was pallor of the face and slight puffiness about the eyes and cheeks, suggestive of Bright's disease except for a translucency of the little folds and wrinkles revealed by close examination. The lips seemed swollen, and the lower was everted

and somewhat pendulous. There was slight œdema of the ankles. His wife had noticed no mental change. Supraclavicular pads were not marked. In the median line of the neck, extending for perhaps two inches above the thyroid cartilage, was a scar, the result of an operation for the removal of a tumor by Dr. Hodges some twelve years ago. Dr. Hodges states that this was a deep-seated lipoma. The texture, color and thickness of the hair had shown no change; pulse 64; temperature 97.5; and the temperature was subnormal whenever taken during the few days which elapsed before treatment was begun. Physical examination, including the blood, gave negative results except as above stated and hæmoglobin 60 per cent. The urine was only 740 c. c. in twenty-four hours; specific gravity 1,020; albumen very faint trace; urea nineteen grammes to the litre; sugar absent; a few medium-sized hyaline casts and abnormal blood corpuscles.

The signs and symptoms seemed to me the same in character as those of myxœdema, though they were less in degree than in any case which I had ever seen or read of; and I had no hesitation in making this diagnosis, in which Dr. J. J. Putnam concurred. Dr. Putnam was so kind as to let me have some of Parke, Davis & Co.'s dried extract of thyroid gland, which had not yet been put on the market; and from April 1st to April 5th, inclusive, fifteen grains, the equivalent of one lobe of a sheep's thyroid, were given twice daily. April 6th, fifteen grains were given once. Before April 6th he complained of pains in the limbs and back. April 10th, seven and a half grains once. The remedy was then omitted until May 5th. After dinner on the evening of April 10th, I was sent for, and found him with severe pain in the cardiac region, resembling that of angina, with quick pulse and tem-

perature slightly above normal. Morphia was given under the skin. For the next two to three weeks now he kept his bed. The attacks of pain tended to recur toward evening, and were always accompanied by marked increase in the pulse-rate, though irregularity and intermittency were never observed. With the subsidence of the pain, either spontaneously or after morphia, the rate promptly fell again. Nitroglycerine had no control over the pain. Repeated and most careful examination of the heart itself failed to detect any change in the size and sounds. He is a courageous man, whose iritic attacks have taught him what pain is, and he is reasonably tolerant of it; but this anginoid pain was so severe as to necessitate morphia hypodermically in one-half-grain doses. Two nights, at least, four of these were required to give relative comfort. The whole cardiac area was tender to pressure or touch, and a very limited spot just outside of the left nipple was exquisitely so. The necessity for hypodermics ceased April 28th. Gradually the attacks of pain diminished and disappeared; as did the tenderness, though more slowly. Meantime the myxœdematous symptoms showed marked improvement. The urine more than doubled in quantity, and April 13th was 1,028 specific gravity, with a very faint trace of albumen and forty-six grammes of urea to the litre, the sediment remaining the same. As he lay in bed now, he kept his arms out, covered only by his night-shirt, and desired only a sheet and one blanket as covering instead of a thick layer as before treatment. Desquamation took place as freely as after scarlet fever, affording the patient much occupation. The skin came off a toe like the finger of a glove. The watering of the eyes and running at the nose diminished materially. May 5th, one-grain doses of the extract every second day were given; May 18th

to June 8th, one grain daily; June 9th to July 5th, two grains daily; from July 6th to the present time, four to eight grains daily. In June he felt better than for a year or two, in fact, perfectly well; and he has since so remained, though with the advent of cold weather the symptoms seem inclined to return in a measure. He has been remarkably free from headaches, to which he was formerly much subject. His weight has not varied materially.

CASE III. Mrs. C, thirty-four years old, consulted me at my office in March, 1893. Her family history was good, except that an uncle was ill for years with "deathly pallor and bloating." The catamenia appeared at fourteen and were regular until her marriage at twenty. Ten months later she was confined, and has never since been pregnant. The catamenia have recurred every five to seven months, painlessly and otherwise normal in every way. For at least ten years she has been notably pale, more or less "bloated," sensitive to cold, perspiring but little if at all, better summers than winters. Six years ago she was operated on for laceration of the cervix, with some subsequent gain in strength. Her urine, she thinks, has not been scanty. She has been supposed to have Bright's disease. She thinks her memory is less good than it was, but recognizes no other mental change. The facies was strongly suggestive of nephritis, but the urine was negative. Unfortunately the urea was not quantitated. There was some swelling of the legs without distinct pitting. Visceral and blood examination gave negative results. The temperature was normal. The skin and its appendages were not notably changed except for swelling and pallor. Supraclavicular pads not marked. At her first visit I was not inclined to think her the subject of myxœdema; but was led to reconsider the diagnosis after my ob-

servation of Case II, which came to me soon after. I therefore sent for her and gave her at first seven and a half grains of the dried extract every third day, after three weeks every second day. There was no unfavorable symptom except some palpitation; later, pains in the limbs were complained of, but they passed off entirely. Improvement was prompt, and has been very marked. The swelling of her face and her girth diminished. There was desquamation of the skin and increase in strength. Early in June she reported that she perspired as she had not done for a long time, and said that all her friends were congratulating her on her changed appearance. One grain of the extract was ordered thrice daily, and this dose has been maintained ever since. I saw her a few days ago; and she then said that she felt better than for years, and has regained her natural shape, though her weight has gone up nearly twenty pounds. Her dressmaker states that her neck measures one-half inch less, her bust three and a half inches less, than last winter. The swelling of the legs has disappeared. The flesh in general has become natural in consistency; there is color in the lips and cheeks. She volunteered the statement that last winter she was not comfortable if the temperature of the room was less than 80° ; and now she objects to a temperature above 65° .

CASE IV. Mr. D., of Missouri, visiting friends in the East, was sent to me by Dr. Gage of Lowell, November 17, 1893; fifty-two years of age, banker. Until five years ago his occupation was a very active one; since then has been sedentary. Family history, previous history and habits good. He never had malaria. For the past two years he has been less strong. The past two winters his hands especially have been very rough, and he has not perspired. Last winter and spring his friends began to notice a change

in his color and appearance. Rest and change of scene was advised; but the panic came, and he had to stay at home. He lost his appetite; bowels became constipated; sexual desire was lost. He was weak, and very sensitive to cold. Some weeks ago he left home and went to some iron springs and then came East. He has gained fifteen pounds in flesh, with increased appetite and strength since leaving home; but his hands and appearance do not change. His eyes water easily, and his tear-ducts were dilated last summer with some relief. His former weight was 205; present, 180. The face presented a dirty pallor, with slightly puffy and translucent lids; no swelling of the lips. The skin generally was harsh, especially the hands and feet. The hair dry; supraclavicular pads marked; temperature 96.5° ; pulse 60; heart sounds weak, otherwise not remarkable; lungs and abdomen clear; knee-jerks present. Blood negative except for diminished hæmoglobin. No enlarged glands; no œdema of the legs; feet objectively very cold. November 17th, the daily amount of urine was about 40 ounces; specific gravity 1,015; an accident prevented the estimation of urea. November 24th, specific gravity 1,020. November 29th, specific gravity 1,025; albumen slightest possible trace; a few casts. December 6th, specific gravity 1,027; albumen slightest possible trace; an occasional hyaline cast. The patient reports a distinct increase in the flow of urine, but the amount has not again been measured. One grain of the thyroid extract twice daily was ordered, and November 29th four grains a day. November 29th, temperature 97.5° ; less watering at eyes; sweat some yesterday after exertion. Some pain and tenderness on right elbow. Increased thyroid extract to six grains a day. December 6th, pulse 72; temperature 97.4° ; skin about the same; color better; less

sensitive to cold; eyes distinctly less watery; is less hoarse than for six months, and sang last Sunday for the first time during that period. The duration of treatment in this case has been very short; but its results confirm the diagnosis. I have learned to push the remedy cautiously.

Cases II, III and IV are unquestionably cases of myxœdema, and can be added to the rapidly lengthening list of cures. Dr. Kinnicutt³ collected 49 cases up to May 1st, treated by thyroid extract; and Dr. R. C. Cabot has kindly collected 68 cases published since May 1st. As before stated, two showed no gain under the treatment. Two of Dr. Murray's⁴ died suddenly while under treatment, the symptoms having markedly improved. One was known, the other suspected to have an unsound heart. Dr. Cabot has found two other fatal cases. In one diarrhœa set in after the first dose, and death was speedy. In the other,⁵ figured in Plate III, in Byrom Bramwell's "Atlas of Clinical Medicine," marked improvement in the myxœdematous symptoms had taken place. January 6, 1892, the patient had an attack of angina, took the last dose, and died seventeen days later. Myocarditis was found at the autopsy. In the 68 cases collected by Dr. Cabot the only other untoward symptoms which occurred often enough to make them especially suggestive were: faintness and headache in six cases, nausea and vomiting in four cases, pain in the back in four cases.

There has been so much written on this subject of late, and it is so prominently before the profession, that I shall not go into statistics or any general con-

³ Transactions of the Association of American Physicians, vol. viii, 1893, p. 332.

⁴ British Medical Journal, 1892, II, p. 450.

⁵ Edinburgh Medical Journal, May, 1893, p. 1014.

sideration of the disease and its symptoms ; but there are several points illustrated by my cases to which I wish to ask your indulgent attention.

In the first place, we must recognize the fact, that, as in all other ailments, there are here differences of degree. Naturally the extreme cases were the first to be recognized, and to these alone does the description as now laid down in the text-books closely apply. Total inactivity or loss of the gland is one thing ; partial inactivity or loss another. It is highly probable that the latter does not necessarily lead to the former ; at all events, a long period of years may elapse before the mild passes into the fully developed disease. The symptoms in Case III were of ten or twelve years' duration ; and yet I at first crossed out myxœdema in my differential diagnosis. Now that our attention is awakened and we are on the lookout for cases, I am convinced that we shall find them to be pretty common. Case IV, the mildest I have seen, I am sure I should not have recognized a year ago, although I was then watching for cases. Case II illustrates the power of the remedy and the dangers of overdosage. Dr. Putnam and I decided on the initial dose in that case, as he had been giving that dose for some time to another, but an extreme, case with great benefit and no untoward result. The anginoid attacks caused me great anxiety. I can now see that it was unwise to fail to appreciate therapeutically differences in degree and duration, but I did not see it then. It may be said in extenuation that knowledge of the safe dosage of the remedy was then very slight and that experience had to be gained. Similar anginoid attacks have been noticed by other observers, and constitute the most important untoward symptom likely to be encountered during treatment. Pains in the limbs and back have also been noticed in some cases, and were complained

of by Case II before the appearance of the anginoid pain. They were also present in Case III, and the pain and tenderness of one elbow in Case IV may be of neuritic nature.

It seems probable that the use of the remedy must be persisted in through life, and that larger doses will be required during the cold than during the hot weather.

Diagnosis should seldom offer any special difficulty at present. Grave anæmias and Bright's disease are readily excluded, as a rule. I say, "as a rule"; for we must not forget Starr's⁶ case, which had been diagnosed as Bright's by eminent authorities and so treated for years. But the albumen and casts disappeared entirely under thyroid extract.

⁶ Transactions of Association of American Physicians, 1893.



